PATENT
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Colleen Coyne — Colleen Coyne

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	David Moore et al.	Art Unit:	1646
Serial No.:	09/365,576	Examiner:	M. Pak
Filed:	August 2, 1999	Customer No.:	21559
Title:	RETINOID X RECEPTOR-INTERACTING POLYPEPTIDES AND RELATED MOLECULES AND METHODS		

Assistant Commissioner for Patents
Washington, D.C. 20231

DECLARATION OF DR. DAVID MOORE UNDER 37 C.F.R. ß 1.131

I, David Moore, declare that:

1. I am an inventor of the invention described and claimed in the above-identified patent application.

2. The present claims of the application recite retinoid X receptor-interacting proteins that have an amino acid sequence that is at least 85% identical to that of RIP15.

3. The other inventors and I conceived of, and reduced to practice, the claimed subject matter of the present application prior to November 10, 1993.

4. The reduction to practice of the claimed invention is evidenced by Exhibits 1 and 2 annexed hereto. The dates of Exhibits 1 and 2 have been redacted in accordance with the standard practice, but are all prior to November 10, 1993. The experiments described and summarized in Exhibits 1 and 2 were performed by Wongi Seol, another inventor of the claimed invention. These experiments were carried out in the United States prior to November 10, 1993.

5. As described in the present application, we performed an *in vivo* interaction trap assay to isolate cDNA molecules encoding proteins that interact with the retinoid X receptor (RXR). For this assay, a mouse cDNA library was introduced into yeast that express a LexA-RXR fusion protein and that contain -galactosidase and LEU2 genes under the control of LexA binding sites. LexA-RXR is not a strong transcriptional activator in yeast. However, LexA-RXR activates expression from LexA binding sites in cells which also express a fusion protein consisting of a transcriptional activation domain joined to another protein which interacts specifically with RXR (as described on pages 12 and 25-27 of the specification).

Clone 15 which encodes RIP15 was isolated in this assay based on its ability to induce expression of both -galactosidase and LEU2, indicating that it encoded a protein that interacted with RXR.

6. Exhibit 1 is a laboratory notebook page that contains a picture of an agarose gel showing the analysis of the plasmid isolated from selected yeast clone 15 and transferred into *E. coli* for analysis (lower panel). The plasmid was purified from *E. coli* and digested with restriction enzymes to determine the size of the cDNA insert in the plasmid. Based on the migration of the restriction enzyme-digested cleavage product in the agarose gel, the cDNA insert was approximately 4.0 kDa (lower left corner of Exhibit 1). A region from this cDNA insert was used as a hybridization probe to isolate the full-length RIP15 coding sequence from a mouse cDNA library, as described on page 27 of the specification.

7. This full-length RIP15 cDNA was sequenced prior to November 10, 1993. Exhibit 2 contains exemplary RIP15 cDNA sequence. In particular, the sequence of primer ip15 PCR 42mer which is listed in Exhibit 2 was designed based on the 5' terminus of this full-length RIP15 cDNA sequence. This primer was used to amplify the RIP15 sequence and add restriction sites flanking the RIP15 sequence to facilitate subsequent subcloning into an expression vector for the production of RIP15 protein. In this primer, the first nucleotide of the second RIP15 codon was altered to generate an NcoI restriction site and Kozak consensus nucleotides were included upstream of the start AUG codon to maximize expression of RIP15 protein. The nucleotides from the RIP15 cDNA sequence that were included in this primer are 5'-CTTCCCCCACAAGTTCTCTG-3'.

8. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are

punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Date: 12/21/01

David Moore, Ph.D.
Professor
Molecular & Cellular Biology
Baylor College of Medicine

Exhibit [redacted]

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RXR- antivey screening

from (P3)
Plasmid isolation from E.coli MC1061/P3 transformant w/ No 1, 2, 5, 6, 7, 101-104, 106, 108, 109, C12 plasmid

each 3 colonies selected for mini prep → digestion w/ HincII

BstXI 2350-80 (cgttrp2/HincII) (850, 2640, 2500, 2250, 3000, 3230, 4700)

→ 2.5/1.3/0.1+X, y+0.12, 0.15, 0.35, 1.7)

[redacted]

(HincII digestion)

EcoRI 2330
BamHI 2985
BstXI 2360/80
RI/BamHI
cgtII 6.65/0.65
vector itself

many ... Vcgttrp2)

(15)

→ Back to yeast transformation No1. No2(=3) No4(=5=6) No7(=8=9) No10(=11=12) No13(=14) No15 No16(=18) No17 No19(=20=24) No23(=24) No25(=26=27) No28(=29) No31(=32=33) No34(=35)

EGY/SH 18-RXR No22 contam? No30 NO DNA No36?

No vector No2 RI/BamHI No5 No6 No7 No101

No103, 104, 107 → just vector itself → forget it → no use

[redacted]

No1 (1)? (2=3)?
No2 (4)=5=6 2.3kb
No5 (7)=8=9 1.9kb
No6 (10)=11 2.0; 12 1.4
No7 (13)=14 2.0; (15) ~4.0

No101 (16)=(17)=18 ~2.0kb
No102 (19)=20=(21) ~1.4; incomplete digestion; No diff. DNA
No105 (28)=29; No DNA
No106 (31)=32=33 1.0kb
No18=104=107 → cgttrp2?
see color?

−9cts → blue
+9cts → Blue.

* 21 needs yeast transformation

V 102 103 104 105 106

Exhibit 2

Brian:

Please make these oligomers. Thanks.

Wongi

p14 PCR 36mer

5' GCG CGC AAG CTT GCC ACC ATG GCC GCG GCA TCG

(AAG CTT: HindIII; ACC ATG GCC: NcoI.)

GCA

p15 PCR 42mer

5' GCG CGC AAG CTT GCC ACC ATG GCT TCC CCC ACA AGT

(AAG CTT: HindIII)

TCT CTG